Remarks

Claims 1-4, 6-11, 13, 16 and 41-44 have been amended. Upon entry of the foregoing amendments, claims 1-16, and 41-44 are pending. No new matter is added by these amendments. Support for the amendments may be found in the original claims and throughout the specification, *e.g.*, at page 17, lines 17–20; page 18, lines 11-15; page 21, line 1 through page 26, line 26; page 46, line 1 through page 48, line 10; and Example 2.

Applicant thanks the Examiner for returning a copy of the initialed Form 1449, which was submitted with Applicant's Reply to Office Action filed on February 27, 2003.

I. Rejections under 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 1-16 and 41-44 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Office Action at page 2. The Office alleges that "[w]hile the specification provides some guidance for a method of determining a probability value for the above listing using the particular equations or values disclosed, the specification does not provide guidance for a method of determining probability by any other means." Office Action at page 3. The office further alleges that "[g]iven the lack of descriptive working examples in the specification, and the unpredictability of generating probability values, the specification as filed is not enabling for any method of determining the listed probability values as claimed. The instant application is only enabled for the above-mentioned computational means of the four probabilities." Office Action at page 3. Applicant respectfully disagrees.

Applicant thanks the Examiner for acknowledging that the specification is enabling for the following equations: initial oligonucleotide probability (p. 21, equation I), transition probability (p. 22, equation II), nucleic acid sequence probability (p. 23, equation III), and probability of each state for the nucleic acid sequence (p. 24, equation IV). Office Action at page 3. Applicant respectfully disagrees, however, with the

Office's allegation that the specification does not enable a person skilled in the art to practice the invention commensurate in scope with the claims.

Disclosure of a single species provides sufficient enabling support if one of skill in the art can, using the state of the art and Applicant's written disclosures, practice the invention in its full scope without undue experimentation.[1] *See In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988); *John Hopkins Univ. v. Cellpro, Inc.*, 152 F.3d 1342, 1361, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998) (Applicant's specification provided sufficient enabling support for the Applicant's claim to immunoassay methods using a generic class of antibodies even though Applicant made a public deposit of only a single hybridoma cell line that secreted a specific antibody); *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1533, 3 U.S.P.Q.2d 1737, 1743 (Fed. Cir. 1987), *cert. denied,* 484 U.S. 954 (1987). Section 2164.03 of the M.P.E.P. states that "[a] single embodiment may provide broad enablement in cases involving predictable factors,[2] such as mechanical or electrical elements." *Citing In re Vickers,* 141 F.2d 522, 526-27, 61 U.S.P.Q. 122, 127 (C.C.P.A. 1944); *In re Cook*, 439 F.2d 730, 734, 169 U.S.P.Q. 298, 301 (C.C.P.A. 1971). Furthermore, it is well established law that patent applicants are not required to disclose every species enabled by their claims. *See In re Vaeck*, 947 F.2d 488, 496, 20 U.S.P.Q.2d 1438, 1445 (Fed. Cir. 1991).

Applicant need only show that one skilled in the art would be able to make and use the claimed invention using the application as a guide. *In re Brandstadter*, 484 F.2d 1395, 1406-07, 179 U.S.P.Q. 286, 294 (C.C.P.A. 1973). In order to be enabling, the

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[1] Applicant notes that the performance of routine and well-known steps cannot create undue experimentation even if it is laborious. *See In re Wands*, 858 F.2d at 737, 8 U.S.P.Q.2d at 1404; *In re. Angstadt,* 537 F.2d 498, 504, 190 U.S.P.Q. 214, 218-219 (C.C.P.A. 1976). Time and difficulty of experiments are not determinative if they are merely routine. M.P.E.P. § 2164.06, page 2100-186.

[2] Applicant respectfully disagrees with the Office's implied assertion that determining probabilities using pre-existing statistical methods is unpredictable. The Office states,"[g]iven the lack of descriptive working examples in the specification, *and the unpredictability of generating probability values,* the specification as filed is not enabling for any method of determining the listed probability values as claimed." Office Action at page 3 (italics added). Applicant respectfully submits that determining probability values using pre-existing statistical methods (*i.e.,* known mathematical equations) is not unpredictable. Applicant respectfully requests that the Office provide legal or other support for the assertion that generating probability values is "unpredictable." Office Action at page 3.

specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well known to those skilled and already available to the public.[3] *See, e.g.,* M.P.E.P. § 2164.05(a), page 2100-185, *citing In re Buchner*, 929 F.2d 660, 661, 18 U.S.P.Q. 2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies*, Inc., 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist and Derrick Co.*, 730 F.2d 1452, 1463, 221 U.S.P.Q. 481, 489 (Fed. Cir. 1984).

Applicant respectfully submits that the specification as filed is enabling for the full scope of the claims. The specification describes, and provides working examples for, the use of inhomogeneous Markov models to determine the probabilities for each of the one or more states for a selected nucleotide. *See, e.g.,* specification at pages 19, line 7 though page 27, line 6, and Examples 1 through 3. As such, specification provides sufficient support to enable one of skill in the art, using the state of the art and the specification disclosure, to practice the invention in its full scope without undue experimentation.

Moreover, although Applicant respectfully maintains that no additional information is needed to enable the full scope of the claims, the specification also provides that "[a]ny probability model applicable to nucleic acid sequence state probabilities can be used for the probability steps if the output of the probability model sufficiently supports the method, including inhomogeneous Markov models having fewer than eight states." *See* specification at page 19, lines 22-24. The specification also points that skilled artisan to Durbin *et al.,* Biological Sequence Analysis (1998), described at page 19, lines 26-27 of Applicant's disclosure.[4] Applicant respectfully asserts that for at least these reasons, the specification as filed provides adequate guidance to enable one of

[3] Applicant respectfully submits that the Office has failed to provide any evidence to suggest that the statistical methods taught by Durbin are not well known in the art. Applicant points the Office to the Bibliography of Durbin, which cites over 200 references written by a diversity of authors. Durbin, pages 326-344.

[4] Copies of the Bibliography of Durbin, as well as Durbin Chapters 5 and 11, are enclosed for the Examiner's convenience. *See* Exhibit A.

skill in the art to practice the invention using additional statistical methods that would be substitutable for the four equations that the Office has determined to be enabled.

Moreover, Applicant respectfully disagrees with the Office's implied assertion that the material referred to in Durbin is "essential material." Office Action at page 4; and Office Action mailed January 13, 2003 at page 5. The M.P.E.P. defines "essential material" as including "that which is necessary to provide an enabling disclosure of the claimed invention." M.P.E.P. § 608.01(p), page 600-79.

Applicant respectfully submits that the material in Durbin is not "essential" because it is not necessary to provide an enabling disclosure of the claimed invention. As stated above, disclosure of a single species provides sufficient enabling support if one of skill in the art can, using the state of the art and Applicant's written disclosures, practice the invention in its full scope without undue experimentation. *See In re Wands*, 858 F.2d at 737; *John Hopkins Univ.*, 152 F.3d at 1361; *Spectra-Physics, Inc*, 827 F.2d at 1533; M.P.E.P. § 2164.03. Furthermore, it is well established law that patent applicants are not required to disclose every species enabled by their claims. *See In re Vaeck*, 947 F.2d at 496.

The Office alleges that "Applicant's reliance on prior art methods may only extend to well known methods and that single specific publications do not support their content as being well known." Office Action at pages 4-5. Applicant disagrees. Applicant reiterates that the Office has not provided evidence to suggest that the methods of Durbin are not well known in the art. *See* footnote 3 *infra*. Applicant respectfully submits that the Office has offered no legal support for the assertion that "single specific publications do not support their content as being well known." Furthermore, Applicant's citation of a single reference, rather than a list of references, cannot properly be used as evidence that the information contained therein is not well known in the art. After all, requiring patent applicants to cite a list of cumulative references would contravene the well-known principle that the specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well known to those skilled and already available to the public. M.P.E.P. § 2164.05(a), page 2100-185.

For at least the foregoing reasons, Applicant respectfully asserts that the specification as filed enables a person of skill in the art to practice the invention commensurate in scope with the claims. Applicant respectfully submits that the rejection of claims 1-16 and 41-44 under 35 U.S.C. § 112, first paragraph is improper and should be withdrawn. Reconsideration and withdrawal of these rejections are respectfully requested.

Should the Examiner maintain this rejection based on the contention that the material disclosed in Durbin is not well known to those of ordinary skill in the art, Applicant respectfully requests that the Examiner support this contention by way of affadavit in accordance with 37 C.F.R. § 1.104 (d)(2).

II. Rejections under 35 U.S.C. § 112, Second Paragraph (Indefiniteness)

Claims 1-16 and 41-44 stand rejected under 35 U.S.C. § 112, second paragraph as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Office Action at page 5.

(a) Rejection of claims 3 and 11

Claims 3 and 11 stand rejected under 35 U.S.C. § 112, second paragraph on the grounds that they contain mathematical equations that are allegedly confusing as they incorporate "'Φ(f)' representing bias which cancels itself out in each equation, and therefore nullifies its effect on the equation." Office Action at page 5. The Office further alleges that "[i]f the Applicant intends this bias not to represented [sic] by the same exact number in the numerator and denominator, then subscripts, or some other form of notation, would be needed in order to clarify this issue." Office Action at page 5. Applicant respectfully disagrees.

Applicant respectfully disagrees that "Φ(f)" (representing bias) cancels itself out of the equation. Applicant respectfully points out that "Φ(f)" corresponds to a function, and as such, "Φ(f)" can have different numerical values corresponding to different elements in the set of states. *See, e.g.,* specification at page 47, lines 13-20. As acknowledged by the Examiner, when "Φ(f)" has different numerical values

corresponding to different elements in the set of states, "Φ(f)" has different values in the numerator and denominator of the equations in claims 3 and 11, and hence "Φ(f)" does not cancel out. *Compare, e.g.,* calculation at page 46, lines 1-5 with calculation on page 48, lines 5-10. Applicant therefore disagrees that bias cancels itself out of the equation.

Applicant also respectfully disagrees with the Office's assertion that subscripts or other notation are required to clarify this issue. Applicant respectfully submits that acceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification. M.P.E.P. § 2173.05(b). Applicant points out that the specification clearly defines "Φ(f)" as a function. *See, e.g.,* specification at page 24, lines 4-5 and lines 18-25. Applicant respectfully submits that one of skill in the art would understand that a function may be assigned different values under different circumstances, and would also understand that Example 2 illustrates that the values substituted for "Φ(f)" do not cancel out of the equation. *Compare, e.g.,* calculation on page 46, lines 1-5, with calculation on page 48, lines 5-10. Applicant therefore respectfully submits that one of skill in the art would understand the meaning of "Φ(f)" in light of the specification, and that no subscripts or notations are necessary to clarify the issue.

For the foregoing reasons, Applicant respectfully asserts that the specification contains guidelines sufficient to teach the meaning of the claim language "Φ(f)" to one of ordinary skill in the art, and thus, the rejection of claims 3 and 11 under 35 U.S.C. § 112, second paragraph is improper and should be withdrawn. Reconsideration and withdrawal of this rejection is respectfully requested.

(b) Rejection of Claims 1, 7, 8, and 41-44

Claim 1 stands rejected under 35 U.S.C. § 112, second paragraph, on the grounds that it recites the phrase "said probability of said nucleic acid sequence" which is allegedly "vague and indefinite due to the lack of clear antecedent basis for the noted phrase in part d) of claim 1." Office Action at page 5. The Office further alleges that "[t]his lack of antecedent basis and unclear wording is also present in other independent claims 7, 8 (regarding part d) said window probability), 41, 42 (part a) probability of a

window), 43, and 44 (part d) said window probability). This rejection is also applicable to claims 2-6 and 9-16 which are claims dependent from said independent claims due to their direct or indirect dependence." Office Action at page 6. Applicant respectfully disagrees.

Applicant disagrees that there is a lack of clear antecedent basis for the phrase "said probability of said nucleic acid sequence." However, in order to facilitate prosecution, Applicant has amended claim 1.

Applicant further disagrees that there is a lack of antecedent basis and unclear wording in claims 7, 8, and 41-44. Applicant respectfully submits that the specification defines "window" as "a contiguous and defined number of nucleotides within a nucleic acid sequence." *See, e.g.,* Specification at page 17, lines 17-20. Applicant also directs the Office to page 25, line 25-26 of the specification, which states "[i]n order to determine the state probabilities for more than one nucleotide, a window is used for each nucleotide that is examined." Applicant therefore submits that one of ordinary skill, reading the claims in light of the specification and in light of his or her knowledge of the art, would understand the meaning of the phrase "said window probability." When read in light of the specification, the phrase "said window probability" is no less understandable than the phrase "said initial oligonucleotide probability." However, in order to facilitate prosecution, Applicant has amended claims 7, 8, 41, and 44.

Applicant therefore submits that the grounds for the rejection of Claim 1, 7, 8, and 41-44 has been rendered moot. Applicant further submits that the amendments to claims 1, 8, and 41-44 has also rendered moot the rejections of dependent claims 2-6 and 9-16. In light of these remarks, Applicant respectfully requests withdrawal of these rejections.

(c) Rejection of Claims 1, 7, 8, and 41-44

Claims 1, 7, 8, and 41-44 stand rejected under 35 U.S.C. § 112, second paragraph, on the grounds that they recites the phrase "based upon" which allegedly renders unclear "the metes and bounds of the parameters that that determine how much basis is included upon the determinations." Office Action at page 6. The Office further alleges that

"[c]laims 2-6 and 9-16 are also indefinite due to their dependency from claims 1 and 8." Office Action at page 6. Applicant respectfully disagrees.

Applicant disagrees that the phrase "based upon" renders unclear the metes and bounds of the claim. However, in order to facilitate prosecution, Applicant has amended claims 1, 7, 8, and 41-44.

Applicant therefore submits that the grounds for the rejection of Claim 1, 7, 8, and 41-44 has been rendered moot. Applicant further submits that the amendments to claims 1, 8, and 41-44 has also rendered moot the rejections of dependent claims 2-6 and 9-16. In light of these remarks, Applicant respectfully requests withdrawal of these rejections.

(d) Rejection of Claim 7

Claim 7 stands rejected under 35 U.S.C. § 112, second paragraph, on the grounds that it recites the term "capable", which allegedly is a relative term that renders the claim indefinite. Applicant respectfully disagrees.

Even if "capable" were a relative term, the use of a relative term does not make a claim *per se* indefinite. *Seattle Box Co. v. Industrial Crating & Packing, Inc.*, 731 F.2d 818, 826, 221 U.S.P.Q. 568, 574 (Fed. Cir. 1984); M.P.E.P. § 2173.05(b). Breadth in a claim is not to be equated with indefiniteness. *In re Miller*, 441 F.2d 689, 169 U.S.P.Q. 597 (C.C.P..A 1971); M.P.E.P. § 2173.04. The words of a claim must be given their plain meaning unless they are defined in the specification. M.P.E.P. § 2111.01, page 2100-47.

For at least these reasons, Applicant submits that Claim 7 is not indefinite in the recitation of "capable." However, in order to facilitate prosecution, Applicant has amended Claim 7. Applicant therefore submits that the grounds for the rejection of Claim 7 has been rendered moot. In light of these remarks, Applicant respectfully requests withdrawal of this rejection.

(e) Rejection of Claims 3 and 11

Claims 3 and 11 stand rejected under 35 U.S.C. § 112, second paragraph, on the grounds that they are allegedly "vague and indefinite due to the lack of clarity in the

following terms: **f**, **S**, $\mathbf{P_f}$, $\mathbf{P_i}$, and $\mathbf{\Phi}$." Office Action at page 7. The Office further alleges that "a clarification of the metes and bounds is required, by listing in the claim the exact definition of each term in order to make clear whether definitions from the art should be utilized or those in the specification since, as argued by Applicant, art defined (not specification defined) methods are apparently heavily relied upon by Applicant." Office Action at page 7. Applicant respectfully disagrees.

The test for determining whether terms in a given claim are indefinite is whether one skilled in the art would understand what is claimed. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991), *cert denied,* 112 S.Ct. 169 (1991). M.P.E.P. § 2173.02 states that "[d]efiniteness of claim language must be analyzed, not in a vacuum, but in light of: (A) The content of the particular application disclosure; (B) The teachings of the prior art; and (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made."

Under M.P.E.P. § 2173.02, the meaning of the terms **f**, **S**, $\mathbf{P_f}$, $\mathbf{P_i}$, and $\mathbf{\Phi}$ must be determined in light of factors (A) through (C) listed above. Applicant respectfully submits that one of skill in the art would understand that **f**, **S**, $\mathbf{P_f}$, $\mathbf{P_i}$, and $\mathbf{\Phi}$ correspond to terms, or parts of terms, of a mathematical equation. Applicant further directs the Office to pages 21-25 of the specification, and Examples 1-2. Applicant respectfully points out that they know of no legal requirement to list "the exact definition of each term" within the claim, and respectfully requests that the Examiner state the legal basis which is relied upon for this statement.

For at least these reasons, Applicant submits that one of ordinary skill in the art, when reading the claim terms **f**, **S**, $\mathbf{P_f}$, $\mathbf{P_i}$, and $\mathbf{\Phi}$ in light of the specification and the teachings of the prior art, would understand what was meant by Claims 3 and 11. Therefore, Applicant respectfully requests that the indefiniteness rejections of claim 3 and 11 under 35 U.S.C. § 112, second paragraph, be withdrawn.

(f) Rejection of Claims 8 and 44

Claims 8 and 44 stand rejected under 35 U.S.C. § 112, second paragraph, on the grounds that they allegedly lack clarity due to the claim language "determining a probability for said window for each of said states. Claims 9-16 are also indefinite due to their dependency from claim 8." Office Action at page 7. Applicant respectfully disagrees.

The Office alleges that "a probability cannot be determined for a window, but rather the states found in the window." Office Action at page 7. Applicant respectfully disagrees. As stated above, under M.P.E.P. § 2173.02, the meaning of the phrase "determining a probability of said window for each of said states" must be determined in light of (A) The content of the particular application disclosure; (B) The teachings of the prior art; and (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. Applicant respectfully submits that the specification defines "window" as "a contiguous and defined number of nucleotides within a nucleic acid sequence." *See, e.g.,* Specification at page 17, line 17. Applicant therefore submits that one of ordinary skill, reading this phrase in light of the specification and his or her knowledge of the art, would understand the meaning of the phrase "determining a probability of said window for each of said states." When read in light of the specification, the phrase "determining a probability of said window for each of said states" is no less understandable than the phrase "determining an initial oligonucleotide probability." However, in order to facilitate prosecution, claims 8 and 44 have been amended.

Applicant respectfully submits that, in light of the above arguments, the grounds for the rejection of Claims 8 and 44 has been overcome or rendered moot. Applicant further submits that the rejections of dependent claims 9-16 has also been overcome or rendered moot. In light of these remarks, Applicant respectfully requests withdrawal of these rejections.

III. Rejections under 35 U.S.C. § 102(b)

Claims 1, 4, 5, 7-9, 12, 13, 15, and 41-44 stand rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Borodovsky *et al.* (Computers Chem., 1993). The Office alleges that "Due to the confusion (see 35 U.S.C. 112, 2nd paragraph rejection above) of "Φ(f)" effectively canceling itself out in the equations of claims 3 and 11, these equations are equivalent to the equations listed on page 129 (Borodovsky *et al.*). Being equivalent equations, if one probability (as provided by Applicant) is "capable of accepting a bias" (claim 7, line 10), then the same probability stated by Borodovsky *et al.* (page 129) must also be capable of accepting a bias. Therefore, Borodovsky *et al.* anticipate the instant invention." Applicant respectfully disagrees.

As noted above, Applicant respectfully disagrees that "Φ(f)" (representing bias) cancels itself out of the equation. Applicant respectfully points out that "Φ(f)" corresponds to a function, and as such, "Φ(f)" can have different numerical values corresponding to different elements in the set of states. *See, e.g.,* specification at page 47, lines 13-20. As acknowledged by the Examiner, when "Φ(f)" has different numerical values corresponding to different elements in the set of states, "Φ(f)" has different values in the numerator and denominator of the equations in claims 3 and 11, and hence "Φ(f)" does not cancel out. For example, Applicant points the Office to Example 2, pages 46-48 of the specification, which illustrates that the values substituted for "Φ(f)" do not cancel out of the equation. *Compare, e.g.,* calculation at page 46, lines 1-5 with calculation on page 48, lines 5-10. Applicant therefore disagrees that bias cancels itself out of the equation.

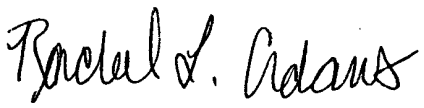
Applicant respectfully disagrees that claims 1, 4, 5, 7-9, 12, 13, 15, and 41-44 are anticipated under §102(b) by Borodovsky. As noted by the Examiner, anticipation under §102(b) requires that every element of a claim appears in a single reference. Applicant respectfully asserts that claims 1, 4, 5, 7-9, 12, 13, 15, and 41-44 each contain the function "Φ(f)" (or the phrase "bias function"), which is lacking in Borodovsky. Applicant respectfully submits that claims 1, 4, 5, 7-9, 12, 13, 15, and 41-44, as amended herein, are therefore not anticipated by Borodovsky. Applicant therefore respectfully requests withdrawal of the rejections under 35 U.S.C. §102(b).

In addition, the Office alleges that "if one claim is 'capable of accepting a bias' (claim 7, line 10), then the same probability stated by Borodovsky *et al.* (page 129) must also be capable of accepting a bias." Office Action at page 8. Applicant respectfully submits that claim 7 has been amended, and that, in light of the amendment of claim 7, the grounds for the rejection of claim 7 have been overcome or rendered moot. In light of these remarks, Applicant respectfully requests withdrawal of the rejection of claim 7.

Conclusion

In view of the above, each of the presently pending claims is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejections of the claims and to pass this application to issue. The Examiner is encouraged to contact the undersigned at (202) 942-5512 should any additional information be necessary for allowance.

Respectfully submitted,



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